

**PATENT** 

# IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Marvin J. FRITZLER

Serial No.: 60/440,326

Filed: January 16, 2003.

For: MONOCLONAL ANTIBODIES TO RNA

**BINDING PROTEIN GW182** 

Group Art Unit: 1642

Examiner: None

Atty. Dkt. No.: UNTI:046USP1

Confirmation No.: 1591

# STATEMENT TO SUPPORT REQUEST FOR CORRECTION OF INVENTORSHIP UNDER 37 C.F.R. §1.48(e)

## MAIL STOP PETITIONS

Commissioner for Patents P. O. Box 1450 Alexandria, VA 22313-1450

- I, Theophany Eystathioy, do declare that:
- 1. I am a citizen of Canada residing at Calgary, Alberta. I currently hold the position of Technology Analyst at University Technologies International. A copy of my *curriculum vitae* is attached.

2. I was incorrectly named as an inventor on the above-captioned provisional application without deceptive invention, and I consent to removal of my name as an inventor thereof.

3. I declare that all statements made herein of my own knowledge are true, and that all statements of my own belief are believed to be true, and further that these statements were made with the knowledge that willful false statements are punishable by fine or imprisonment, or both, under §1001 of Title 18 of the United States Code.

March 26, 2008

Date

Commissioner for Patents April 21, 2008

#### **CURRICULUM VITAE**

## THEOPHANY EYSTATHIOY

#### PERSONAL PROFILE

## Contributions:

- ❖ successfully completed: 16 publications, and 24 published abstracts
  - o utilize strong time management and prioritization skills
- manage 3 students and 2 technicians
  - o effectively demonstrate interpersonal, communication and organizational skills
- coordinate/direct multiple projects:
  - o GW bodies in breast cancer, skin cancer, neurons, glia and stem cells
  - o the study of metabolomics in Rheumatic disease
  - o demonstrate strong problem solving and literature review skills
- teach and communicate science in a fun, engaging and interactive manner to:
  - o grade 8 to university graduate students
  - o nurses
  - o conference presentations
    - awarded "overall merit- most outstanding presentation" at the Canadian Rheumatology Association in 2002

## Skills:

- strong technical and analytical skills
  - o technologies previously utilized include (not an exhaustive list):
    - immunoprecipitation
    - Western, Northern, Southern blot analysis
    - Transfection reactions
    - Protein-protein interactions
    - Addressable laser bead immunoassay
    - Tissue culture
    - Elisa assay
    - Immunofluorescence
    - Mass spectrometry
    - 1D, 2D protein SDS-PAGE gels
    - RT-PCR, PCR
    - RNA interference technology: siRNA, miRNA
    - Use a variety of databases including: NCBI PubMed, and the subsets of ExPASy proteomics server

# I. BIOGRAPHICAL DATA

Date of Birth: February 01, 1973 Citizenship: CANADIAN

Permanent address: Calgary, Alberta

teystath@ucalgary.ca Email:

Ph.D. Cellular and Molecular Biology Degree:

Medical Sciences Program

Faculty of Medicine University of Calgary

Adjunct Assistant Professor Position:

Division of Rheumatology Department of Medicine

University of Calgary (02/2006 - present)

## II. ACADEMIC RECORD:

1) Graduate:

Ph.D. Cellular and Molecular Biology, University of Calgary, 2004. Dr. M.J Fritzler (supervisor)

Thesis: GW182 is a novel protein that localizes to a unique cytoplasmic compartment

M.Sc. Biochemistry and Molecular Biology, University of Calgary, 1998. Dr. K. latrou (supervisor)

Thesis: The ecdysone-induced regulatory cascade in the silkmoth ovary: The HR3 and E75 genes.

# 2) Undergraduate:

B.Sc. Cellular Molecular and Microbial Biology, University of Calgary, 1994.

# III. SPECIAL RESEARCH TRAINING:

- 1) Research Associate- University of Calgary, April 2005- January 2006 Department of Medicine, University of Calgary, with Dr. M.J Fritzler
- Postdoctoral Associate-University of Florida, October 2004 March 2005 Departments of Oral Biology and Anatomy & Cell Biology, University of Florida, Gainesville, FL, USA with Dr. E.K.L Chan
- 3) Research Assistant- University of Calgary, March-August, 2000 Department of Medicine, University of Calgary, with Dr. M.J Fritzler research focused on autoimmune diseases
- 4) Research Assistant- The Scripps Research Institute, La Jolla, California. October, 1998-February, 2000 Department of Molecular and Experimental Medicine with Dr. E.K.L. Chan research focused on autoimmune diseases
- 5) Research Assistant- University of Calgary, July, 1994-December, 1994, Department of Biochemistry and Molecular Biology with Dr. K. latrou. research focused on the developmental process of oogenesis

## IV. Teaching experience

 Medical Science 351 undergraduate Honors Cell and Molecular Biology Winter 2007

Coordinator Dr. Mayi Arcellana-Panlilio

- -Cell cycle (2 lectures, 2hrs each)
- -Cell signaling (2 lectures, 2hrs each)
- -provided examination questions and participated in student evaluation
- 2) Medical Science 351 undergraduate Honors Cell and Molecular Biology Winter 2006

Coordinator Dr. Mayi Arcellana-Panlilio

- -special lecture RNAi (1 lecture, 2hrs each)
- -Cell cycle (2 lectures, 2hrs each)
- -Cell signaling (2 lectures, 2hrs each)
- -provided examination questions and participated in student evaluation
- 3) MDSC 683.02 -Cancer Biology (CB8)- Molecular mechanisms of Cancer graduate level course: Winter 2006
  - Coordinator Dr. D. Fujita
  - -1 lecture on miRNA (40 min)
  - -provided examination questions and participated in student evaluation
- 4) MDSC 639.02 –IMM-3: Autoimmunity and Immunodeficiency graduate level course: Fall 2006
  - Coordinator Drs Julie Deans and Robert Bell
  - -1 lecture on systemic autoimmunity (1hr)
  - -provided examination questions and participated in student evaluation

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- 5) Participated in
  - a) the Galileo Educational network at the University of Calgary (Contact Dr. Sharon Friesen): videoconference with Grade 8 students from Edmonton and Nanton on our research work.
  - b) March 10, 2006 guest speaker at Calgary Girls School in April, 2006: (contact: Nancy Turnbull Grade 8 Math/Science Teacher Calgary Girls' School) c) gave a presentation to the nurses part of HMRC in-service (asked by Carolyn Robertson <a href="mailto:croberts@ucalgary.ca">croberts@ucalgary.ca</a>) to talk about breast cancer and GWBs on January 15, 2007
- 6) Teaching assistant- Course: Medical Sciences 717 Gene cloning and recombinant DNA technology. May-June, 1997, University of Calgary

# V. AWARDS AND DISTINCTIONS:

Award/Distinction	Awarded by	Year Held/value
HFSP fellowship award	HFSP (Carine Schmitt, cschmitt@hfsp.org)	April 2005- 1year, renewable for one more year, to work with Dr. Walter Reith (Geneva, Switzerland) -declined due to unforeseen relocation
EMBO long-term fellowship award	EMBO (Liselott.Ahlgren@embo. org)	December 2004- received for 1year (65,000 + benefits), 1year, renewable for one more year, to work with Dr. Walter Reith (Geneva, Switzerland) -declined due to unforeseen relocation
University Technologies International Inc. Fellowship in Medicine	University Technologies International Inc	January 01-December 31, 2003/ \$15,000
Graduate Research Scholarship	Medical Science Graduate Education Committee, University of Calgary	September 2002-April 2003/ \$6000
Certificate and Cash award for "Most Outstanding presentation Award"	Canadian Rheumatology Association in Lake Louise, Alberta	February 21, 2002 / \$500
Fee Scholarship	Faculty of Medicine Trust Fund, University of Calgary	September, 2001/ \$3,000

Graduate Research Scholarship	Biochemistry and Molecular Biology Graduate Education Committee. University of Calgary	1) September-December, 1997/ \$3920 2) September-December, 1996/ \$3920 3) January-April, 1996/ \$3920
Dean's list	University of Calgary	Fall/Winter1993-1994
The University of Calgary matriculation merit award	University of Calgary	1990/value approx. \$1000

# VI. Paper chosen by the Faculty of 1000 (www.facultyof1000.com)- evaluated May 2002

Eystathioy, T., Chan, E. K.L., Tenenbaum, S. A., Keene, J.D., Griffith, K., and Fritzler, M.J. 2002. A phosphorylated cytoplasmic autoantigen, GW182, associates with a unique population of human mRNAs within novel cytoplasmic speckles. Molecular Biology of the Cell. 13: 1338-1351

# VII. Peer-reviewed publications

- 1. Moser, J.J., Eystathioy, T., Chan, E.K.L., and Fritzler, M.J. 2007. Human glioblastoma and glia cell GW bodies are enriched with proteins involved in mRNA degradation, stabilization and RNAi. Glia. *submitted*
- 2. Jakymiw, A., Pauley, K.M., Li, S., Ikeda, K., Lian, S., Eystathioy, T., Satoh, M., Fritzler, M.J., and Chan, E.K.L. 2007. The role of GW/P bodies in RNA silencing. J. Cell Sci. *in press*
- 3. Pauley, K., Eystathioy, T., Jakymiw, A., Hamel, J.C., Fritzler, M.J., and Chan, E. K.L. 2006. GW body formation is linked to microRNA maturation. EMBO R. 7: 904-910
- 4. Lian, S., Jakymiw, A., Eystathioy, T., Hamel, J., Fritzler, M., and Chan, E.K.L. 2005. GW bodies, microRNAs, and the cell cycle. Cell cycle. 5: 242-5.
- 5. Jakymiw, A., Lian, S., Eystathioy, T., Satoh, M., Hamel, J., Fritzler, M., and Chan, E.K.L. 2005. GW bodies are essential for mammalian RNA interference. Nature Cell Biol. 12: 1167-74.
- 6. Yang, Z., Jakymiw, A., Wood, M.R., Eystathioy, T., Rubin, R.L., Fritzler, M.J., and Chan, E.K.L. 2004. GW182 is critical for the stability of GW bodies expressed during the cell cycle and cell proliferation. J. Cell Science. 117: 5567-78
- 7. Stinton, L.M., Eystathioy, T., Selak, S., Chan, E.K.L., Fritzler, M.J. 2004. Autoantibodies to Cytoplasmic Organelles: Endosomes, Lysosomes, Golgi

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- Complex, Centrosomes, Proteasomes, Assemblyosomes, Exosomes and GW Bodies. Clinical Immunology. 110: 30-44
- 8. Eystathioy, T., Jakymiw, A., Chan, E.K.L., Seraphin, B., Cougot, N., and Fritzler, M.J. 2003. The GW182 protein co-localizes with mRNA degradation associated proteins hDcp1 and hLSm4 in cytoplasmic GW bodies. RNA. 9:1171-1173
- 9. Eystathioy, T., Chan, E.K.L., Takeuchi, K., Mahler, M., Luft, L.M., Zochodne, D.W., and Fritzler, M.J. 2003 Clinical and serological associations of autoantibodies to GW bodies and a novel cytoplasmic autoantigen GW182. Journal of Molecular Medicine 81: 811-818
- Eystathioy, T., Chan, E.K.L., Mahler, M., Luft, L.M., Fritzler, M.L., and Fritzler, M.J. 2003. A panel of monoclonal antibodies to cytoplasmic GW bodies and the mRNA binding protein GW182. Hybridoma and Hybridomics. 22: 79-86
- 11. Swevers, L., Eystathioy, T., and latrou, K. 2002. The Orphan Nuclear Receptors BmE75A and BmE75C of the Silkmoth Bombyx mori: Hormonal Control and Ovarian Expression. Insect Biochem Mol Biol. 12:1643-1652
- 12. Fritzler, M.J., Hanson, C., Miller, J., and Eystathioy, T. 2002. Specificity of autoantibodies to SS-A/Ro on a transfected and overexpressed human 60 kDa Ro autoantigen substrate. Journal of Clinical Laboratory Analysis 16: 103-108
- 13. Eystathioy, T., Chan, E. K.L., Tenenbaum, S. A., Keene, J.D., Griffith, K., and Fritzler, M.J. 2002. A phosphorylated cytoplasmic autoantigen, GW182, associates with a unique population of human mRNAs within novel cytoplasmic speckles. Molecular Biology of the Cell. 13: 1338-1351
- 14. Eystathioy, T., Peebles, C.L., Hamel, J. C., Vaughan, J. H., and Chan, E.K.L. 2002. Autoantibody to hLSm4 and the heptameric LSm complex in anti-Sm sera. Arthritis and Rheumatism. 46: 726-734
- 15. Eystathioy, T., Swevers, L., and latrou, K. 2001. The orphan nuclear receptor BmHR3A of Bombyx mori: hormonal control, ovarian expression and functional analysis. Mechanisms of Development 103: 107-115
- 16. Eystathioy, T., Jakymiw, A., Fujita, D.J., Fritzler, M.J. and Chan, E.K.L. 2000. Human autoantibodies to a novel Golgi protein Golgin-67: high similarity with golgin95/gm130 autoantigen. Journal of Autoimmunity 14:179-187
- 17. Jakymiw, A., Raharjo, E., Rattner, J.B., Eystathioy, T., Chan, E.K.L., and Fujita, D.J. 2000. Identification and characterization of a novel Golgi protein, Golgin-67. Journal of Biological Chemistry 275:4137-4144

## VIII. Posters/Abstracts

- Bhanji, R., Eystathioy, T., Chan, E.K.L., and Fritzler, M.J. 2007. The majority of patients with autoantibodies to GWBs have neuropathies and/or Sjögren's Syndrome. 62<sup>nd</sup> annual Canadian Rheumatology Association Meeting. Lake Louise, Alberta
- Weljie, A., Martin M., Fritzler, M.J., Vogel, H.J., LeClercq, S., Walker, J., and Eystathioy, T. 2007. Metabolite biomarkers of scleroderma elucidated using 1H NMR metabolomics. 62<sup>nd</sup> annual Canadian Rheumatology Association Meeting. Lake Louise, Alberta
- Songqing Li, Han, F., Lian, S., Jakymiw, A., Eystathioy, T., Fritzler, M.J., and Chan, E.K.L. 2007. GW182: the molecular and structural link between RNAi and mRNA decapping. Keystone symposium. MicroRNAs and siRNAs: Biological functions and mechanisms. Keystone, Colorado
- 4. Eystathioy, T., Pauley, K., Jakymiw, A., Hamel, J., Fritzler, M.J., and Chan, E.K.L. 2005. MiRNA is an important factor in GW body formation. 45<sup>th</sup> Annual ASCB meeting. San Francisco, California.
- Jakymiw, A., Lian, S., Eystathioy, T., Satoh, M., Hamel, J., Fritzler, M., and Chan, E.K.L. 2005. Disassembly of GW bodies disrupts mammalian RNA interference. 45<sup>th</sup> Annual ASCB meeting. San Francisco, California.
- Moser, J.J., Eystathioy, T., Zochodne, D., and Fritzler, M.J. 2005. GWBs in neurons contain proteins involved in mRNA degradation and RNAi. Biochemistry and molecular biology retreat (University of Calgary). Banff, Alberta.
- 7. Bhanji, R.A., Eystathioy, T., Chan, E.K.L., and Fritzler, M.J. 2005. hAgo2 is a major autoantigen in patients with anti-GWB Antibodies. Biochemistry and molecular biology retreat (University of Calgary). Banff, Alberta.
- 8. Jakymiw, A., Eystathioy, T., Satoh, M., Hamel, J., Fritzler, M., and Chan, E.K.L. 2005. Disruption of GW bodies impairs RNA interference. Ninth International Workshop on Autoantibodies and Autoimmunity. Gainesville, Florida.
- 9. Shangli, L., Songqing, L., Jakymiw, A., Eystathioy, T., Fritzler, M.J., Chan, E.K.L. 2005. Intracellular dynamics of GW bodies foci of mRNA degradation and siRNA activity. Ninth International Workshop on Autoantibodies and Autoimmunity. Gainesville, Florida.
- 10. Shangli, L., Songqing, L., Jakymiw, A., Eystathioy, T., Fritzler, M.J., Chan, E.K.L. 2005. Intracellular dynamics of GW bodies foci of mRNA degradation and siRNA activity. 10<sup>th</sup> Annual Meeting of the RNA Society. Banff, Alberta, Canada. Poster.

- 12. Stinton, L., Eystathioy, T., Selak, S., Luft, L., and Fritzler, M. 2004.
  Autoantibodies to cytoplasmic "somes": endosomes, lysosomes, proteasomes, assemblyosomes, exosomes and GW bodies. Canadian Rheumatology Association Annual Meeting. Lake Louise, Alberta. Poster
- 13. Luft, L. M., Chan, E.K.L., Eystathioy, T., and Fritzler, M.J. 2004. The use of autoantibodies to a novel mRNA-binding protein, GW182, to study the dynamics and role of a novel cytoplasmic compartment in malignancy. 12<sup>th</sup> International Congress of Immunology. Montreal, Canada. Poster
- 14. Eystathioy, T., Jakymiw, A., Chan, E.K.L., and Fritzler, M.J. 2003. The GW182 protein co-localizes with mRNA degradation associated proteins Dcp1 and LSm4 in GW bodies. 8<sup>th</sup> Annual Meeting of the RNA Society. Vienna, Austria. Poster
- 15. Eystathioy, T., Chan, E.K.L., Yang, Z., Takeuchi, K., and Fritzler, M.J. 2002. The novel cytoplasmic mRNA-binding phosphoprotein GW182 is a target of autoantibodies from patients with Sjogren's syndrome and other conditions. American College of Rheumatology. New Orleans. Poster
- 16. Eystathioy, T., Peebles, C.L., Vaughan, J.H., and Chan, E.K.L. Human anti-Sm antibodies recognize LSm4 and LSm heptameric complex. American College of Rheumatology Annual Meeting, Philadelphia, 2000, Arthritis Rheum. 43:S327 Poster.
- 17. Jakymiw, A., Raharjo, E., Rattner, J.B., Eystathioy, T., Chan, E.K.L., and Fujita, D.J. Characterization of a new Golgi protein, golgin-67, that associates with SRC kinase. Oncogene and Growth Control Meeting, La Jolla, 1999.
- 18. Swevers, L., Eystathioy, T., Dinnetz, I., Ito, K., and Iatrou, K. Ovarian development in Lepidopteran insects: The silkmoth Paradigm. Third International Symposium on Molecular Insect Science: Snowbird Utah, USA, 1998.
- 19. Swevers, L., Eystathioy, T., Ito, K., and Iatrou, K. The ecdysone response in the silkmoth ovary. Gordon Research Conference on Molecular Biology of the egg: Andover New Hampshire, USA, 1998.
- 20. Swevers, L., Eystathioy, T., and latrou, K. The ecdysone response in the follicular cells of the silkmoth ovary during pupal and pharate development. IV International Workshop on The Molecular Biology and Genetics of Lepidoptera: Crete, Greece 1997.

- 21. Swevers, L., Eystathioy, T., and latrou, K. Analysis of the ecdysone response in the follicular epithelium of the silkmoth ovary during pupal and pharate adult development. 13<sup>th</sup> International Congress, 56<sup>th</sup> SDB Annual Meeting-Developmental Biology: Snowbird, Utah, 1997.
- 22. Eystathioy, T., Swevers, L., and latrou, K. Isolation and ovarian expression of ecdysone-inducible genes in Bombyx mori. Northwest Regional Developmental Biology Conference: Friday Harbor, Washington, 1997.
- 23. Swevers, L., Cherbas, L., Cherbas, P., Lunke, M., Qian, H., Eystathioy, T., and latrou, K. Nuclear hormone receptors in the silkmoth, Bombyx mori, and their role in ovarian development. Annales d'Endocrinologie: Rouen-France, 1996.
- 24. Swevers, L., Qian, H., Kendirgi, F., Eystathioy, T., Lindstrom-Dinnetz, I., and latrou, K. terminal differentiation of ovarian follicular cells in the silkmoth Bombyx mori: molecular switches controlling a complex regulatory pathway. XX International Congress of Entomology: Florence, Italy, 1996.

# IX. Conference Presentations

- 1. 2005 Biochemistry and Molecular Biology Retreat. Banff, Alberta, 2005. GW body formation is linked to microRNA maturation. Eystathioy, T., Pauley, K., Jakymiw, A., Hamel, J.C., Fritzler, M.J., and Chan, E. K.L.
- 2. 2005 Ninth International Workshop on Autoantibodies and Autoimmunity. Gainesville, Florida. September, 2005. *Invited speaker* GW bodies are cytoplasmic foci committed to microRNA processing. Eystathioy, T., Pauley, K., Jakymiw, A., Hamel, J.C., Fritzler, M.J., and Chan, E. K.L.
- 3. 2004 Canadian Rheumatology Association Annual Meeting. Lake Louise, Alberta. February, 2004.
  Clinical associations and epitopes bound by autoantibodies to GW bodies and the cytoplasmic autoantigen GW182.
  Eystathioy, T., Luft, L., Chan, E.K.L., and Fritzler, M.J. (presentation given by L. Luft)
- 4. 2002 Canadian Rheumatology Association: Lake Louise, Alberta. February 20-23, 2002.

Molecular characterization of a novel cytoplasmic protein GW182 and the identification of a unique cytoplasmic compartment.

- T. Eystathioy, E.K.L. Chan, K. Griffith, and M.J Fritzler.
- 5. 1997 Northwest Regional Developmental Biology Conference: Friday Harbor, Washington. March 13-15, 1997 Isolation and ovarian expression of ecdysone-inducible genes in Bombyx mori.

 1997 Department of Medical Biochemistry retreat: Western Heritage Centre, Cochrane, Alberta. October 4, 1997.
 Molecular Biology of Oogenesis in Lepidoptera

X. References: available upon request